REMARKS

The Examiner has rejected claims 1-8, 30 and 31 a second time under 35 U.S.C 103(a) as being unpatentable over the Salvesen et al. reference in light of STN Registry File No. 17590-01-1 and Stedman's Medical Dictionary (Twenty-Second Edition, 1972; p.377) each cited to show facts, in view of Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; ppp.420-426) not having been persuaded by Applicants' arguments. The Salvesen reference shows that the amphetaminil racemate has a general stimulant effect and that four stereoisomeric configurations exist as identified by chromatographic separation and isolated from thin layer chromatography spots

Regarding point (1) of the Examiner's arguments (pg 12) the Examiner contends that it is generally expected that one of a group of isomers would have more activity than the other isomers. However, the Applicants' point is not that it may have more activity but that the isomer exhibited the unexpected result of having more activity and of possessing fewer adverse side effects. The composition of the invention not only has an optimal therapeutic effect but also lacks potentially dangerous side effects associated with the administration of the racemate. The invention shows a greater stimulant effect compared with the racemate and fewer stereotypy-associated side effects. Therefore the simultaneous increase in activity and decrease in toxicity is surprisingly and unexpectedly advantageous. A skilled artisan would have expected the exact opposite, ie that a compound's toxicity would increase with its increased therapeutic effect. These are not predictable results. Furthermore, the Applicants spent a considerable amount of time attempting to purify the isomers and had issues of degradation whenever the isomers were isolated.

Applicants contend that such results are not at all predictable. Resolved isomers have been found to be of equal therapeutic effect, have been found to have different biological activities, and some are inactive. Frequently, the isolated isomers show a less optimal therapeutic effect compared with the racemate.

Regarding Examiner's Response to Applicants' Arguments starting on pg 15 Applicants do not agree that the Salvesen et al. reference teaches that the two diastereometric mixtures derived from amphetaminil show a general stimulant effect or that one of the diastereometric mixtures has more activity than the other. Examiner's position is that it would be obvious to then identify the isomer with the greatest activity in view of her interpretation of the Salvesen et al. reference.

The Applicants believe that the Salvesen et al. reference shows the investigation of the configuration of the isomers and their presence in commercial samples of the amphetaminil racemate and that the amphetaminil racemate breaks down in the commercial preparation described. The Applicants' point is not that one isomer may have more activity than the other isomers but that the isomer exhibited the unexpected result of having more activity and possessing fewer adverse side effects. The composition of the invention not only has an optimal therapeutic effect but also lacks potentially dangerous side effects associated with the administration of the racemate. The invention shows a greater stimulant effect compared with the racemate and fewer stereotypy-associated side effects. Therefore the simultaneous increase in activity and decrease in toxicity is surprisingly and unexpectedly advantageous. A skilled artisan would have expected the exact opposite, ie that a compound's toxicity would increase with its increased therapeutic effect. These are not predictable results.

Applicants furthermore are not claiming an isomeric mixture rather a single isomer, (R,R'),(R,S')-amphetaminil sulfate or another pharmaceutically-acceptable salt thereof, substantially free of (S,R'), (S,S')-amphetaminil. There is no teaching, motivation or suggestion in the Salvesen et al. reference to make the purified (R,R"),(R,S")-amphetaminil. In fact the Salvesen et al. reference teaches away from the present invention by showing that the amphetaminil racemate degrades over time in commercial dragees and that the isomers/diastereometric mixtures are unstable.

In view of the above, Applicants do not believe the Salvesen reference predicts, teaches, suggests or motivates the present invention either in light of STN Registry File No. 17590-01-1 which shows the structure of amphetaminil and or in light of Stedman's Medical Dictionary which shows that dragees are sugar-coated pills or capsules, or in light of Remington's Pharmaceutical Sciences which shows that drugs are chemically modified to alter the duration of action of a drug; to modify the transportation and distribution of the drug in the body; to reduce toxicity; and to overcome difficulties encountered in pharmaceutical formulation procedures or in the dosage form itself.

Applicants believe that the claimed invention is patentably distinct from the references cited by the Examiner and that the foregoing remarks place the claims in condition for allowance. No new matter has been introduced by these amendments. No fees are believed due for an extension of time due to the filing of this paper.

Any questions about this response should be addressed to Karen Guerrero. The telephone number is 610-933-2490.

Sincerely,

Karen Guerrero

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